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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/705,926 | 11/13/2003 | Pavel Slanina | SYN-0036 | 7713 |

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EXAMINER

MOORE, SUSANNA

ART UNIT PAPER NUMBER

1624

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/705,926 | Applicant(s) SLANINA ET AL. | |
| | Examiner Susanna Moore | Art Unit 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 November 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 14-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>12/8/04, 8/18/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

In view of the restriction requirement, Applicant has elected group (I), claims 1-13, which are drawn to compounds of formula (3) and (7).

Applicant's election with traverse of group (I) in the reply filed on 11/21/2005 is acknowledged. The traversal is on the ground(s) that the Examiner failed to establish distinctness. This is not found persuasive because a process of synthesis or method of use is considered a separate and distinct invention than the corresponding products.

The said inventions are distinct for the following reasons:

Inventions (I) and (II) are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the process of making an oxime from a ketone is well-known and is used in the field of chemistry with a variety of substrates, e.g. the antiallergy agents synthesized by Carr et. al. (U.S. 3,946,022).

Inventions (I) and (II) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product

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as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the compound of formula 3 can be alkylated with different substrates to produce a variety of compounds, e.g. dopamine D2 and serotonin 2A antagonist (WO 2005066165).

Claim Objections

Claim 9 is objected to because of the following informalities: the word “of” should be placed between “amount” and “said”. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

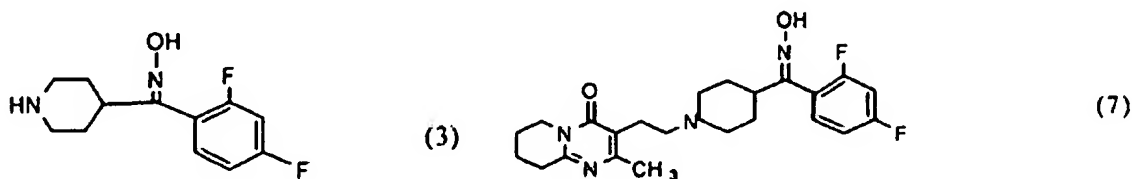
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 9-11, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Marquillas Olondriz et. al. (ES 2050069).

The rejected claims are drawn to making enriched Z-isomer oxime 7 in greater than 80% yield; followed by a cyclization reaction to produce risperidone.



The Specification on page 10 states, “An enriched Z-isomer oxime of formula (3) and (7) can also be obtained by conversion of the E-isomer oxime into the Z-isomer form. Specifically, by heating the E-isomer, typically a mixture of the Z- and E-isomers, in a solvent, the E-isomer is converted into the Z-isomer. More specifically, the undesired E-isomer is converted into the E-isomer of the oxime...by heating in an inert solvent...at a sufficient temperature, preferably, higher than 80°C.”

The Specification also states on page 7, “Because of the discovery that the E-isomer oxime is not merely slower reacting than the Z-isomer oxime but rather is essentially unreactive,...”

Marquillas Olondriz et. al. teaches the reaction of the oxime intermediate 7 to the cyclized product, risperidone, with sodium in refluxing THF. See column 6, example 9, lines 60-67, and column 7, lines 1-28, and the final cyclized product, column 7, example 10, lines 30-47 and column 8, lines 1-15.

As the Specification says the enrichment occurs on “heating in an inert solvent” this heating inherently produced the enrichment.

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In addition, Marquillas Olondriz et. al. must have had the oxime enriched with the Z-isomer to obtain a yield of 87.7% of the cyclized product. Applicant discloses on page 7 of the Specification that the E-isomer is “unreactive” due to the orientation of the hydroxyl group pointing away from the fluoro substituent. Thus, the Z-isomer must have been present in the oxime mixture in excess of 90, since most cyclized reactions do not go to 100% yield.

Claims 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Kennis et. al. (US 4,804,663).

Kennis et. al. teaches the synthesis of oxime 3 under basic conditions in refluxing water followed by the cyclization of oxime 3. See column 11, lines 1-17 and column 12, lines 10-25.

The inherency argument mentioned above applies here as well. Thus, claims 9-12 are anticipated by Kennis et. al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strupczewski et. al. (U.S. 4,408,054).

The current invention teaches the process of making and use of acetic acid salts of oximes (3) and (7).

Strupczewski et. al. teaches compounds of salts of oxime (3). The compound 4-(2,4-difluorobenzoyl)-piperidine oxime is used in example 25, column 26, lines 66-67. This oxime intermediate is used for the exact same utility, the cyclization to the corresponding benzoisoxazole.

The difference between the prior art and the current invention is that the prior art reference uses the free base of compound (3) while Applicant uses the acetic acid salt of compound (3).

Claim 1 of the prior art references claims the oxime (3) "or salts thereof." See paragraph bridging columns 38 and 39. The only definition of salts is found in column 10, lines 61-68 of the patent, which lists 9 different pharmaceutically acceptable salts. Acetic acid is one of the salts mentioned, and therefore, acetic acid would be an obvious choice to use for compound (3).

The compound, 4-(2,4-difluorobenzoyl)-piperidine oxime, is used for the same utility in the reference as in the current invention, the synthesis of risperidone. The same sequence of reactions occurs, where the oxime is cyclized intramolecularly to the benzoisothiazole in refluxing water as the solvent. See column 27, lines 16-39. This heating does the enrichment.

The inherency argument mentioned above applies here as well. Thus, claims 1-8 are obvious over the teachings of Strupczewski et. al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susanna Moore whose telephone number is (571) 272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


SM

Mark L. Berch
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